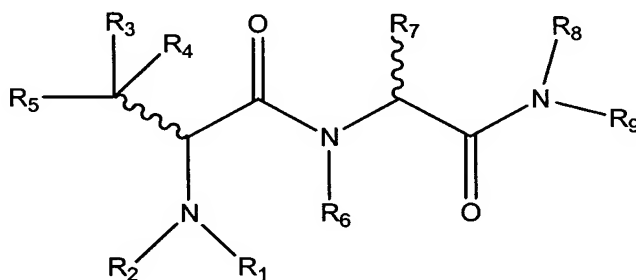


**We claim:**

1. A method of treating, inhibiting the growth of, or eradicating a tumor in a mammal in need thereof wherein said tumor is resistant to at least one chemotherapeutic agent which method comprises providing to said mammal an effective amount of a compound of Formula (II):



II

10

wherein:

- R<sub>1</sub> is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-

- R<sub>2</sub> is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>,

-O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-

5 R-;

or R<sub>1</sub> and R<sub>2</sub> taken together with the nitrogen atom to which they are attached is a three to seven membered ring;

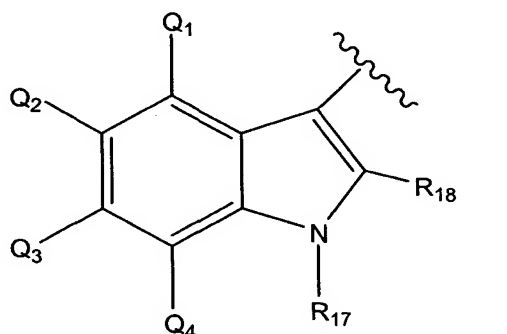
10 R<sub>3</sub> is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, 15 Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

20 R<sub>4</sub> is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, 25 -Cl, -F, -CN, -CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

30 or R<sub>3</sub> and R<sub>4</sub> taken together with the carbon to which they are attached form a three to seven membered ring;

R<sub>5</sub> is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>,  
 5 -O<sub>2</sub>CR<sub>10</sub>, -SH, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; aryl-R- and aryl and provided that when R<sub>5</sub> is an indolyl moiety of the formula

10



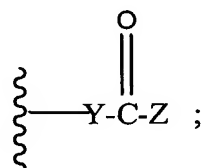
R<sub>17</sub> is H or an optionally substituted alkyl or acyl group; and  
 R<sub>18</sub>, Q<sub>1</sub>, Q<sub>2</sub>, Q<sub>3</sub>, and Q<sub>4</sub> are independently selected from H, halogen, alkyl,  
 15 acyl, -OH, -O- alkyl, -O-acyl, -NH<sub>2</sub>, -NH-alkyl, -N(alkyl)<sub>2</sub>, -NH-acyl, -NO<sub>2</sub>, -SH, -S-alkyl and -S-acyl, wherein the alkyl and acyl groups of the substituents are optionally substituted;

R<sub>6</sub> is selected from the group consisting of H; a saturated or unsaturated  
 20 moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>,  
 25 -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

$R_7$  is selected from the group consisting of a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

$R_8$  is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

$R_9$  is:



and wherein,

R is a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>,

-NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group;

5

X is a moiety selected from the group consisting of: -OH, -OR, =O, =S, -O<sub>2</sub>CR, -SH, -SR, -SOCR, -NH<sub>2</sub>, -NHR, -N(R)<sub>2</sub>, -NHCOR, -NRCOR, -I, -Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CO<sub>2</sub>R, -CHO, -COR, -CONH<sub>2</sub>, -CONHR, -CON(R)<sub>2</sub>, -COSH, -COSR, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR, and -SO<sub>2</sub>R;

10

Aryl is an aromatic ring selected from the group consisting of: phenyl, naphthyl, anthracyl, phenanthryl, thienyl, furyl, indolyl, pyrrolyl, thiophenyl, benzofuryl, benzothiophenyl, quinolyl, isoquinolyl, imidazolyl, thiazolyl, oxazolyl, and pyridyl, optionally substituted with R or X;

15

Y is a moiety selected from the group consisting of: a linear, saturated or unsaturated, one to six carbon alkyl group, optionally substituted with R, ArylR-, or X; and,

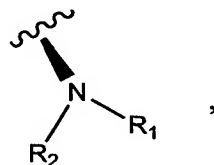
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Z is a moiety selected from the group consisting of: -OH, -OR; -SH; -SR; -NH<sub>2</sub>; -NHR; -N(R)<sub>2</sub>; -NHCH(R<sub>11</sub>)COOH; and -NRCH(R<sub>11</sub>)COOH, wherein R<sub>11</sub> is a moiety having the formula: R, or -(CH<sub>2</sub>)<sub>n</sub>NR<sub>12</sub>R<sub>13</sub>, wherein n =1-4 and R<sub>12</sub> and R<sub>13</sub> are independently selected from the group consisting of: H; R; and -C(NH)(NH<sub>2</sub>);

25

with the provisos that:

(1) when R<sub>1</sub> is H and R<sub>2</sub> is CH<sub>3</sub> of the moiety



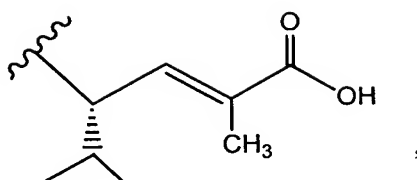
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R<sub>3</sub> is CH<sub>3</sub>, R<sub>4</sub> is CH<sub>3</sub>, R<sub>5</sub> is phenyl, R<sub>6</sub> is H, R<sub>8</sub> is CH<sub>3</sub>,

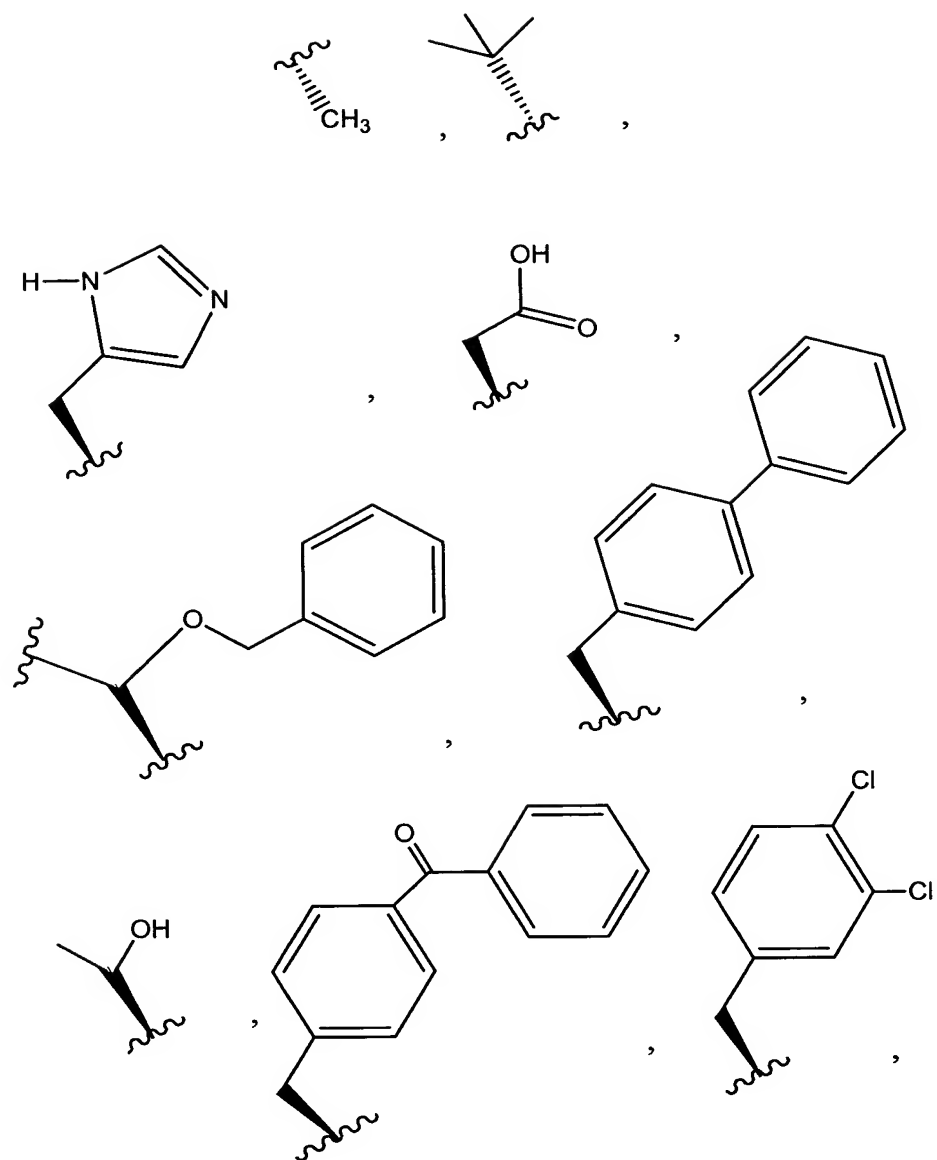
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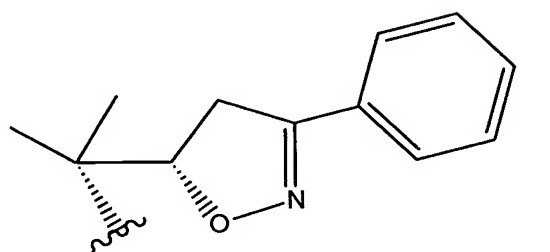
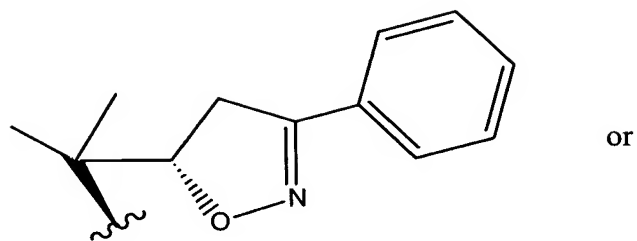
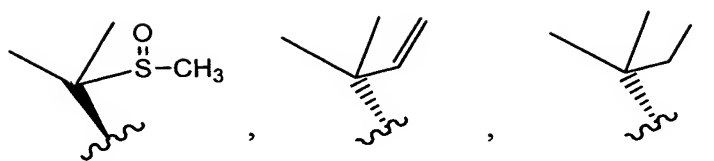
a) when  $R_9$  is

5

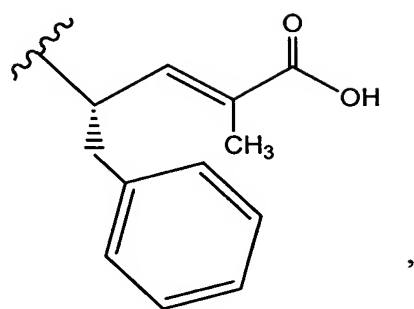


then  $R_7$  is not





b) when  $R_9$  is

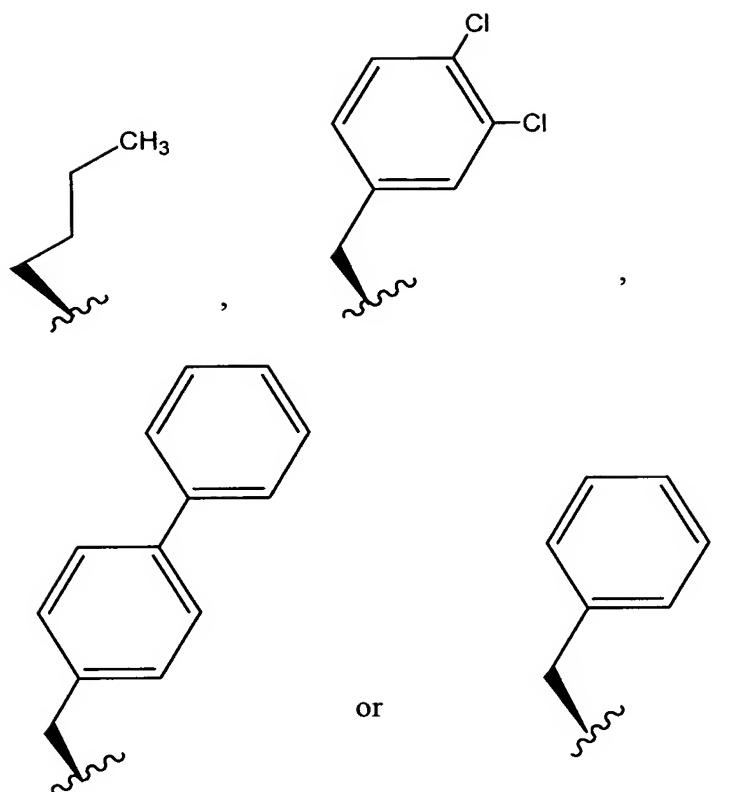


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then  $R_7$  is not

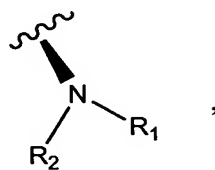
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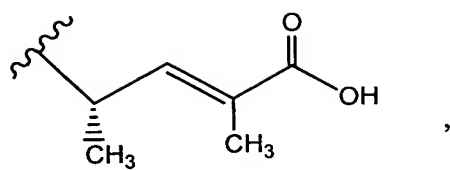
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(2) when  $R_1$  is H and  $R_2$  is  $\text{CH}_3$ , of the moiety



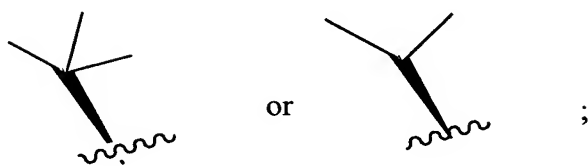
10  $R_3$  is  $\text{CH}_3$ ,  $R_4$  is  $\text{CH}_3$ ,  $R_5$  is phenyl,  $R_6$  is H,  $R_8$  is H,

a)  $R_9$  is



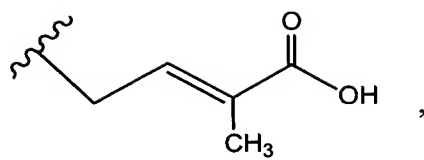
then R<sub>7</sub> is not

5



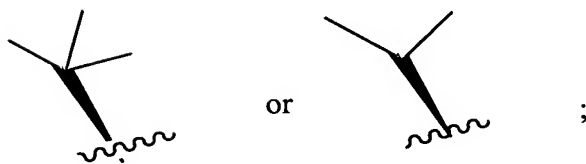
b) when R<sub>9</sub> is

10



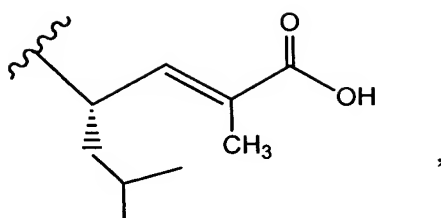
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then R<sub>7</sub> is not



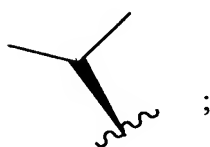
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c) when  $R_9$  is



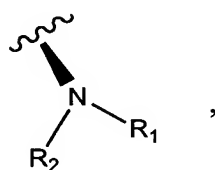
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then  $R_7$  is not



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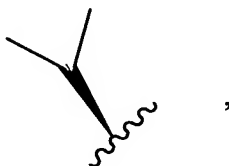
(3) when  $R_1$  is H and  $R_2$  is  $\text{CH}_3$ , of the moiety



15

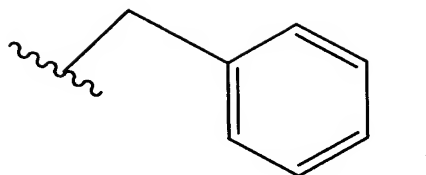
$R_3$  is  $\text{CH}_3$ ,  $R_4$  is  $\text{CH}_3$ ,  $R_5$  is phenyl,  $R_6$  is H,

$R_7$  is



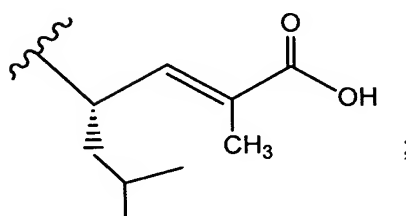
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$R_8$  is



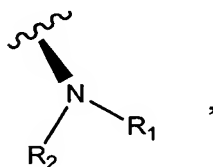
then  $R_9$  is not

5



10

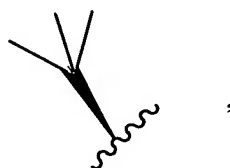
(4) when  $R_1$  is H,  $R_2$  is H, of the moiety



$R_3$  is  $CH_3$ ,  $R_4$  is  $CH_3$ ,  $R_5$  is phenyl,  $R_6$  is H,

15

$R_7$  is

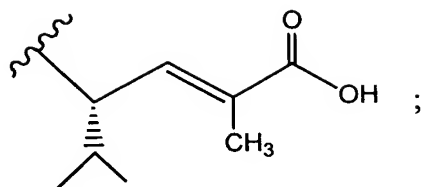


and

$R_8$  is  $CH_3$ ,

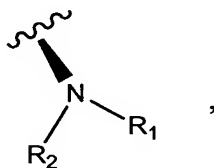
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then R<sub>9</sub> is not



5

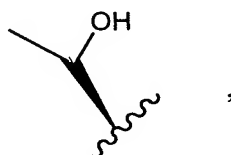
(5) when R<sub>1</sub> is H and R<sub>2</sub> is CH<sub>3</sub> of the moiety



R<sub>3</sub> is CH<sub>3</sub>, R<sub>4</sub> is CH<sub>3</sub>, R<sub>5</sub> is phenyl, R<sub>6</sub> is H,

10

R<sub>7</sub> is

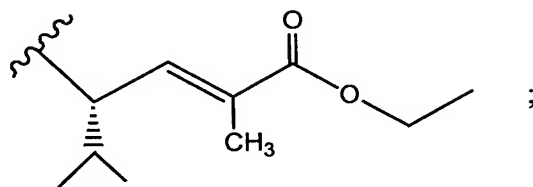


and

R<sub>8</sub> is CH<sub>3</sub>,

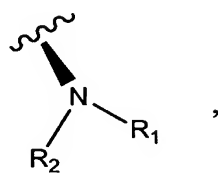
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then R<sub>9</sub> is not



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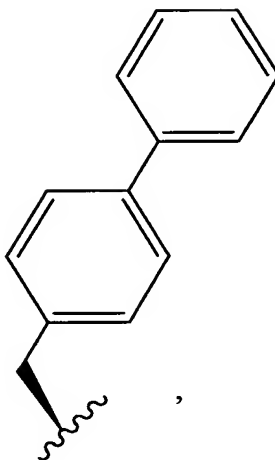
(6) when  $R_1$  is H and  $R_2$  is  $\text{CH}_3$  of the moiety



$R_3$  is  $\text{CH}_3$ ,  $R_4$  is  $\text{CH}_3$ ,  $R_5$  is phenyl,  $R_6$  is H,

5

$R_7$  is



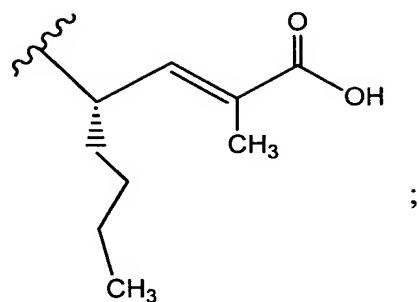
and

$R_8$  is  $\text{CH}_3$ ,

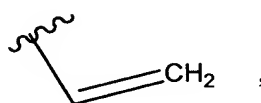
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then  $R_9$  is not

15



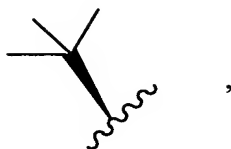
(7) when  $R_1$  is H,  $R_2$  is H,  $R_3$  is  $\text{CH}_3$ ,  $R_4$  is  $\text{CH}_3$ ,  $R_5$  is



5

$R_6$  is H,

$R_7$  is

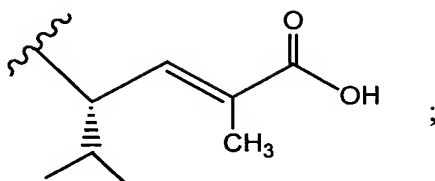


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and

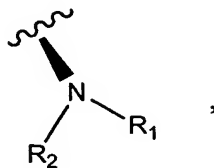
$R_8$  is  $\text{CH}_3$ ,

15 then  $R_9$  is not



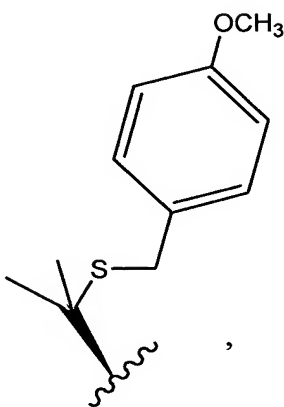
20

(8) when  $R_1$  is H and  $R_2$  is  $\text{CH}_3$ , of the moiety



5  $R_3$  is  $\text{CH}_3$ ,  $R_4$  is  $\text{CH}_3$ ,  $R_5$  is phenyl,  $R_6$  is H,

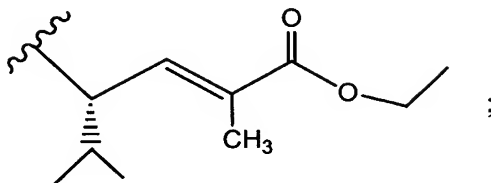
$R_7$  is



and

10  $R_8$  is  $\text{CH}_3$ ,

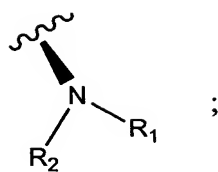
then  $R_9$  is not



15

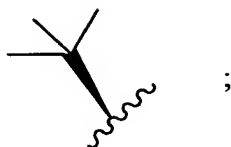
(9) when  $R_1$  is H and  $R_2$  is  $\text{CH}_3$  of the moiety





R<sub>3</sub> is CH<sub>3</sub>, R<sub>4</sub> is CH<sub>3</sub>, R<sub>5</sub> is phenyl,  
R<sub>6</sub> is H,

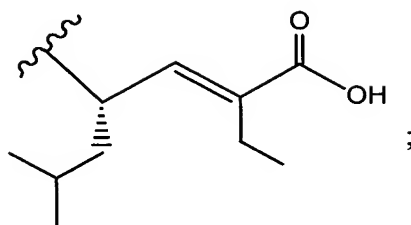
5 R<sub>7</sub> is



and

R<sub>8</sub> is H,

10 then R<sub>9</sub> is not



15

(10) when R<sub>1</sub> is H, R<sub>2</sub> is CH<sub>3</sub>,

20

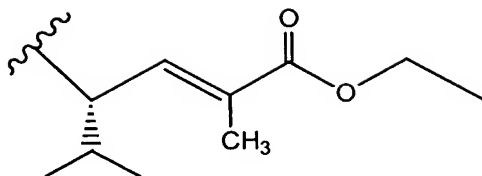
R<sub>3</sub> is H, R<sub>4</sub> is phenyl, R<sub>5</sub> is phenyl,  
R<sub>6</sub> is H,

$R_8$  is  $\text{CH}_3$ ,

and

$R_9$  is

5



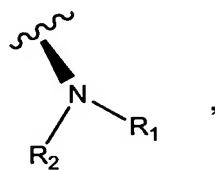
10

then  $R_7$  is not



15

(11) when  $R_1$  is H and  $R_2$  is  $\text{CH}_3$  of the moiety



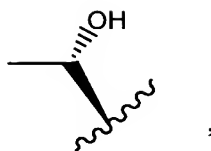
$R_3$  is  $\text{CH}_3$ ,  $R_4$  is  $\text{CH}_3$ ,  $R_5$  is phenyl,

20  $R_6$  is H,

$R_8$  is  $\text{CH}_3$ ,

and

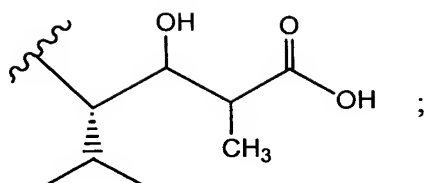
$R_7$  is



5

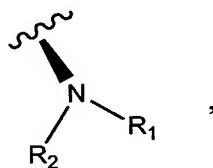
then  $R_9$  is not

10



15

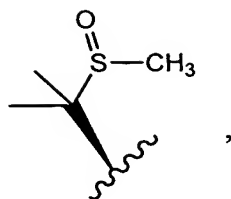
(12) when  $R_1$  is H and  $R_2$  is  $\text{CH}_3$  of the moiety



$R_3$  is  $\text{CH}_3$ ,  $R_4$  is  $\text{CH}_3$ ,  $R_5$  is phenyl,

20  $R_6$  is H,

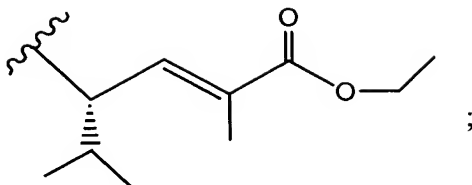
$R_7$  is



and

$R_8$  is  $\text{CH}_3$ ,

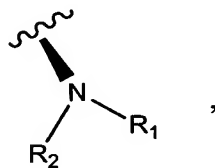
5 then  $R_9$  is not



10

15

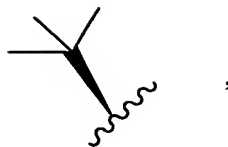
(13) when  $R_1$  is H and  $R_2$  is  $\text{CH}_3$  of the moiety



$R_3$  is  $\text{CH}_3$ ,  $R_4$  is  $\text{CH}_3$ ,  $R_5$  is phenyl,

20  $R_6$  is H,

R<sub>7</sub> is

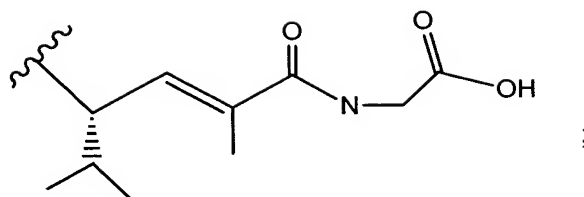


and

R<sub>8</sub> is CH<sub>3</sub>,

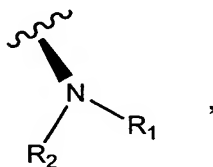
5

then R<sub>9</sub> is not



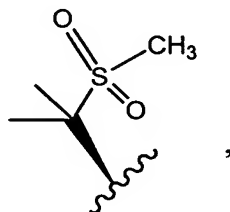
10

(14) when R<sub>1</sub> is H and R<sub>2</sub> is CH<sub>3</sub> of the moiety



15 R<sub>3</sub> is CH<sub>3</sub>, R<sub>4</sub> is CH<sub>3</sub>, R<sub>5</sub> is phenyl,  
R<sub>6</sub> is H,

R<sub>7</sub> is

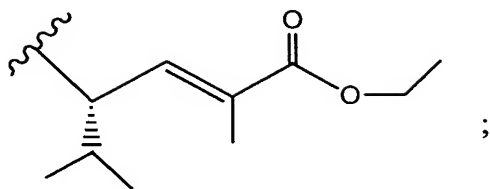


20 and

$R_8$  is  $\text{CH}_3$ ,

then  $R_9$  is not

5



10

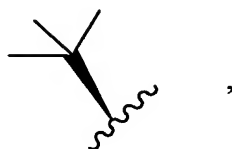
(15) when  $R_1$  is  $\text{CH}_3$ ,  $R_2$  is H,

$R_3$  is H,  $R_4$  is phenyl,  $R_5$  is phenyl,

$R_6$  is H,

15

$R_7$  is



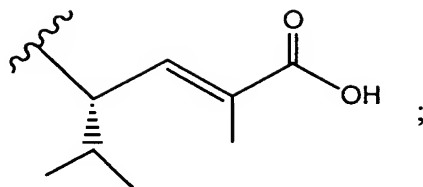
and

$R_8$  is  $\text{CH}_3$ ,

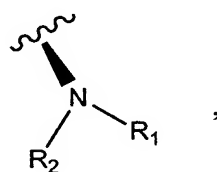
20

then  $R_9$  is not

25



5 (16) when  $R_1$  is  $\text{CH}_3$  and  $R_2$  is H of the moiety

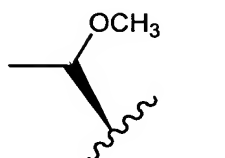


$R_3$  is  $\text{CH}_3$ ,  $R_4$  is methyl,  $R_5$  is phenyl,

$R_6$  is H,

10

$R_7$  is

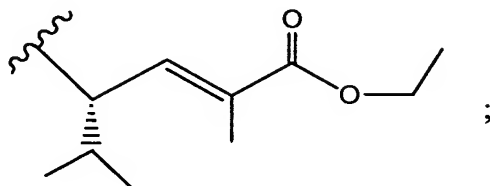


and

$R_8$  is  $\text{CH}_3$ ,

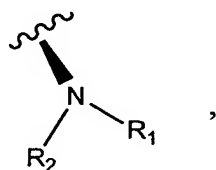
15

then  $R_9$  is not



20

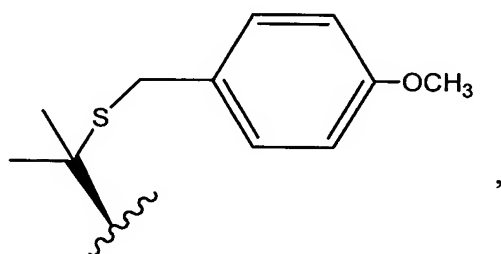
(17) when  $R_1$  is  $\text{CH}_3$  and  $R_2$  is H of the moiety



5

$R_3$  is  $\text{CH}_3$ ,  $R_4$  is methyl,  $R_5$  is 4-methoxyphenyl,  
 $R_6$  is H,

$R_7$  is



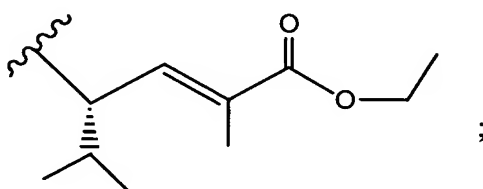
10

and

$R_8$  is  $\text{CH}_3$ ,

then  $R_9$  is not

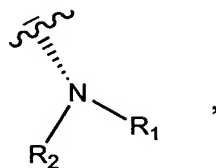
15



20



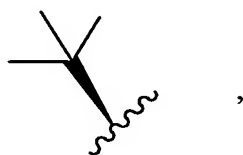
(18) when  $R_1$  is  $\text{CH}_3$  and  $R_2$  is H of the moiety



$R_3$  is  $\text{CH}_3$ ,  $R_4$  is  $\text{CH}_3$ ,  $R_5$  is 3-chlorophenyl,

5  $R_6$  is H,

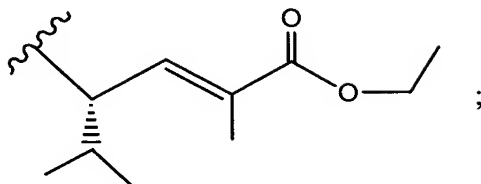
$R_7$  is



and

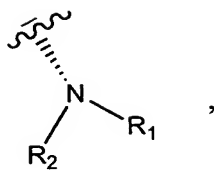
10  $R_8$  is  $\text{CH}_3$ ,

then  $R_9$  is not



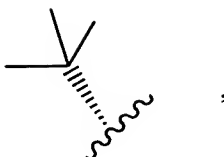
15

20 (19) when  $R_1$  is  $\text{CH}_3$  and  $R_2$  is H of the moiety



$R_3$  is  $\text{CH}_3$ ,  $R_4$  is  $\text{CH}_3$ ,  $R_5$  is phenyl,  
 $R_6$  is H,

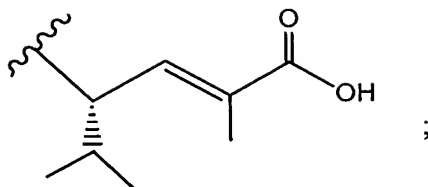
5  $R_7$  is



and

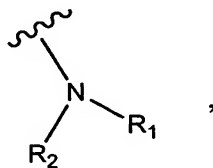
$R_8$  is  $\text{CH}_3$ ,

10 then  $R_9$  is not



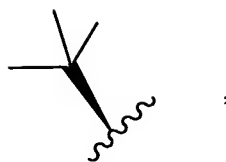
15

(20) when  $R_1$  is  $\text{CH}_3$  and  $R_2$  is  $\text{CH}_3$  of the moiety



20  $R_3$  is H,  $R_4$  is H,  $R_5$  is 3-pyridyl,  
 $R_6$  is H,

R<sub>7</sub> is

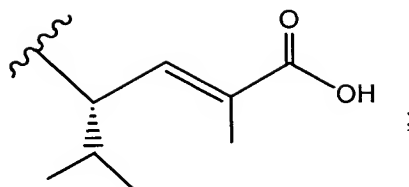


and

5 R<sub>8</sub> is CH<sub>3</sub>,

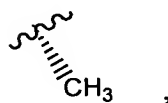
then R<sub>9</sub> is not

10



15

(21) when R<sub>1</sub> is CH<sub>3</sub> and R<sub>2</sub> is H, R<sub>3</sub> is

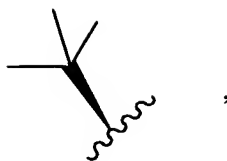


20

R<sub>4</sub> is H, R<sub>5</sub> is -O-CH<sub>2</sub>-phenyl,

R<sub>6</sub> is H,

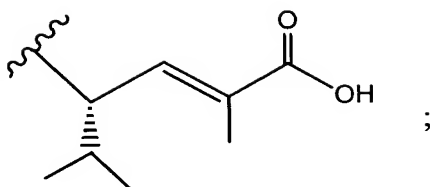
R<sub>7</sub> is



and

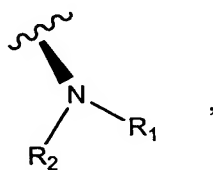
$R_8$  is  $\text{CH}_3$ ,

5 then  $R_9$  is not



10

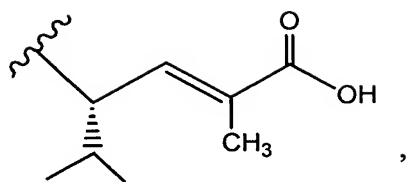
15 (22) when  $R_1$  is H and  $R_2$  is  $\text{CH}_3$  of the moiety



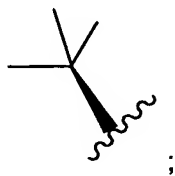
$R_3$  is  $\text{CH}_3$ ,  $R_4$  is  $\text{CH}_3$ ,  $R_5$  is phenyl,  $R_6$  is  $\text{CH}_3$ ,  $R_8$  is  $\text{CH}_3$ ,

and

20  $R_9$  is



then  $R_7$  is not



(23) when  $R_1$  is H;

5

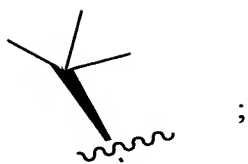
$R_3$  and  $R_4$  are  $\text{CH}_3$ ;

$R_5$  is phenyl;

10

$R_6$  is H;

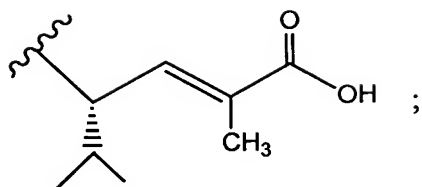
$R_7$  is



15

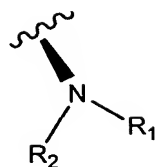
$R_8$  is  $\text{CH}_3$ ;

$R_9$  is



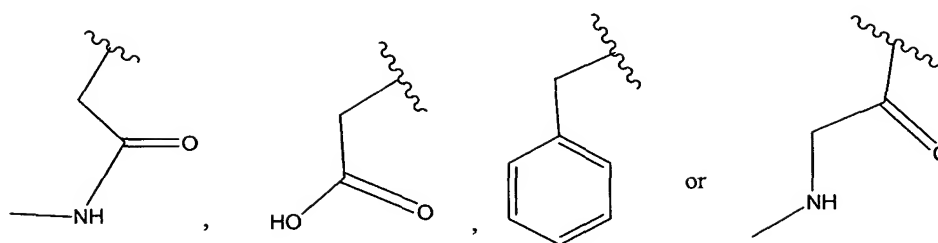
20

then R<sub>2</sub> of the moiety



5

is not



10

or pharmaceutically acceptable salts thereof.

15 2. The method according to Claim 1 wherein the chemotherapeutic agents are antimicrotubule inhibitors.

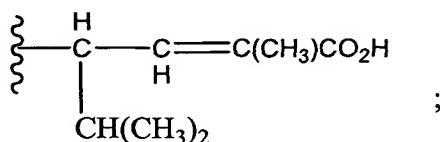
3. The method according to Claim 2 wherein the antimicrotubule inhibitors are selected from the group consisting of paclitaxel, docetaxel, vinblastine, vincristine  
20 and vinorelbine.

4. The method according to claim 1 wherein the tumors are selected from the group consisting of breast, colon, lung, prostate, melanoma, epidermal, leukemia, kidney, bladder, mouth, larynx, esophagus, stomach, ovary, pancreas, liver, skin and brain.

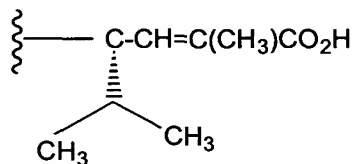
25

5. The method according to Claim 1 wherein the tumors overexpress MDR-1, MXR or MRP.
6. The method according to Claim 1 wherein the resistance to chemotherapeutic agents is multiple drug resistance (MDR).
7. The method according to Claim 1 wherein the resistance is inherent or acquired.
8. The method according to Claim 7 wherein the resistance is acquired.
9. The method according to Claim 1 wherein a compound of Formula (II) is administered before, concurrently, or after treatment with the chemotherapeutic agent.
10. The method according to Claim 1 wherein:
- (a)  $R_1$  and  $R_2$  are independently: H, methyl, ethyl, propyl, or n-butyl; or
- (b)  $R_1$  and  $R_2$  taken together with the nitrogen atom to which they are attached form a three to six membered ring;
11. The method according to Claim 10 wherein  $R_1$  and  $R_2$  are independently: H or  $CH_3$ .
12. The method according to Claim 11 wherein  $R_1$  is H and  $R_2$  is  $CH_3$ .
13. The method according to Claim 10 wherein no more than one of  $R_1$  and  $R_2$  is H.
14. The method according to Claim 1 wherein  $R_3$  and  $R_4$  are independently: H, methyl, ethyl, n-propyl or n-butyl, provided no more than one of  $R_3$  and  $R_4$  is H or,  $R_3$  and  $R_4$  are joined to form a  $\beta$ -cyclopropyl,  $\beta$ -cyclobutyl,  $\beta$ -cyclopentyl or  $\beta$ -cyclohexyl ring.
15. The method according to Claim 14 wherein  $R_3$  and  $R_4$  are each methyl.
16. The method according to Claim 1 wherein  $R_5$  is cyclohexyl, phenyl, naphthyl, thienyl, anthracyl, pyrrolyl or indolyl.

17. The method according to Claim 16 wherein  $R_5$  is phenyl, or indolyl.
18. The method according to Claim 17 wherein  $R_5$  is phenyl;
19. The method according to Claim 1 wherein  $R_6$  and  $R_8$  are independently: H or methyl.
- 5 20. The method according to Claim 19 wherein  $R_6$  is H and  $R_8$  is methyl.
21. The method according to Claim 1 wherein  $R_7$  is a three to six carbon, branched alkyl group.
22. The method of Claim 21 where  $R_7$  is  $-C(CH_3)_3$ .
23. The method of Claim 1 wherein; Z is OH, or  $-OR_{14}$ ;  $R_{14}$ , is a linear or branched one to six carbon alkyl group,  $-NHCH(R_{11})COOH$  or  $-NCH_3CH(R_{11})COOH$ ;  $R_{11}$  is R, or  $-(CH_2)_n NHC(NH)(NH_2)$ ; or
- 10  $R_9$  is  $-C(R_{15})-C=C(R_{16})C(O)-OH$  wherein  $R_{15}$  is methyl, ethyl, n-propyl, isopropyl, tert-butyl, iso-butyl, or sec-butyl and  $R_{16}$  is H, methyl, ethyl, propyl, iso-propyl, n-butyl, iso-butyl or sec-butyl.
- 15 24. The method according to claim 1 wherein  $R_9$  is:



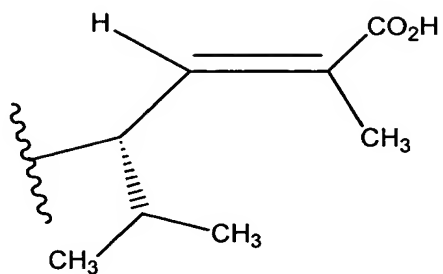
25. The method according to Claim 1 wherein
- 20  $R_9$  is



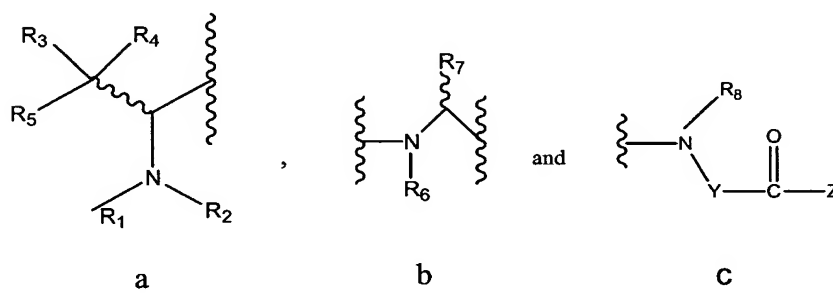


26. The method according to Claim 1 wherein  $R_9$  is:

5



10 27. The method according to Claim 1 wherein the absolute configurations of moieties a, b and c of Formula (II) are:



15 are selected from:

	<u>a</u>	<u>b</u>	<u>c</u>
	S	S	S
	R	S	S
and	S	S	R.

20

28. The method according to claim 1 wherein said compound of Formula (II) is selected from:

3-Chloro-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide ,

5 4-Chloro-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

4-chloro-N, $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10 4-Chloro-N, $\beta$ , $\beta$ -triethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

4-Chloro-N, $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

15 N, $\beta$ , $\beta$ ,3-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

20 N, $\beta$ , $\beta$ ,3-tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ ,3-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25 N, $\beta$ , $\beta$ ,3-Tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ ,4-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

30 N, $\beta$ , $\beta$ ,4-tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ ,4-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-  
N<sup>1</sup>,3-dimethyl-L-valinamide,

- 5 N, $\beta$ , $\beta$ ,4-Tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-  
N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ ,3,4-Pentamethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-  
methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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N, $\beta$ , $\beta$ ,3,4-pentamethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-  
oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 15 N, $\beta$ , $\beta$ ,3,4-Pentamethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-  
N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ ,3,4-Pentamethyl-D-phenylalanyl-N<sup>1</sup>,[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-  
N<sup>1</sup>,3-dimethyl-L-valinamide,

- 20 N, $\beta$ , $\beta$ ,3,5-Pentamethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-  
methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ ,3,5-pentamethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-  
oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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N, $\beta$ , $\beta$ ,3,5-Pentamethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-  
N<sup>1</sup>,3-dimethyl-L-valinamide,

- 30 N, $\beta$ , $\beta$ ,3,5-Pentamethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-  
N<sup>1</sup>,3-dimethyl-L-valinamide,

N-Methyl-3-(2-thienyl)-L-valyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-  
oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N-methyl-3-(2-thienyl)-D-valyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 5 N-Methyl-3-(2-thienyl)-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N-Methyl-3-(2-thienyl)-D-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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N-Methyl-3-thien-3-yl-L-valyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 15 N-methyl-3-thien-3-yl-D-valyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N-Methyl-3-thien-3-yl-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 20 N-Methyl-3-thien-3-yl-D-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-(1-Benzothien-3-yl)-N-methylvalyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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3-(1-Benzothien-3-yl)-N-methylvalyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 30 3-(1-Benzothien-2-yl)-N-methylvalyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-(1-Benzothien-2-yl)-N-methylvalyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

4-tert-Butyl-N, $\beta$ , $\beta$ -trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 5 4-tert-Butyl-N, $\beta$ , $\beta$ -trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N-Ethyl- $\beta$ , $\beta$ -dimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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N-Ethyl- $\beta$ , $\beta$ -dimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 15 N-(tert-Butoxycarbonyl)-N- $\beta$ , $\beta$ ,2-tetramethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,  $\beta$ , $\beta$ ,2-tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 20 N,  $\beta$ , $\beta$ ,2-Tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ ,2-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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N, $\beta$ , $\beta$ ,2-Tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 30 3-bromo-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-bromo-N, $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-phenyl-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-phenyl-N, $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10 N, $\beta$ , $\beta$ -trimethyl-3-vinyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-ethyl-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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4-bromo-N, $\beta$ , $\beta$ -trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

4-phenyl-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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4-carboxy-N, $\beta$ , $\beta$ -trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25 3-Methoxy-N, $\beta$ , $\beta$ -trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-Hydroxy-N, $\beta$ , $\beta$ -trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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N,3-Dimethyl-4-phenyl-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,3-dimethyl-4-phenyl-D-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

(2E,4S)-4-[[[(2S)-2-[[[(2S)-3,3-dimethyl-2-(methylamino)octanoyl]amino}-3,3-dimethylbutanoyl](methyl)amino]-2,5-dimethyl-2-hexenoic acid,

(2E,4S)-4-[[[(2S)-2-[[[(2R)-3,3-dimethyl-2-(methylamino)octanoyl]amino}-3,3-dimethylbutanoyl](methyl)amino]-2,5-dimethyl-2-hexenoic acid,

10 N,N,β,β-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N-(2-hydroxyethyl)-N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

15 2-Methoxy-N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

20 2-Methoxy-N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,O,β,β-tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25 N,O,β,β-tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

2-Methoxy-N,O,β,β-tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

30 2-Methoxy-N,O,β,β-tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-Fluoro-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

5 3-Fluoro- N, $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ -Trimethyl-3-(trifluoromethyl)-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10 N, $\beta$ , $\beta$ -Trimethyl-3-(trifluoromethyl)-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3,5-Difluoro-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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3,5-Difluoro-N, $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ -trimethyl-3,5-bis(trifluoromethyl)-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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N, $\beta$ , $\beta$ -trimethyl-3,5-bis(trifluoromethyl)-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25 O-isopropyl-N, $\beta$ , $\beta$ -trimethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

O-isopropyl- N, $\beta$ , $\beta$ -trimethyl-D-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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3-Cyclohexyl-N-methyl-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

5 (2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-2-(methylamino)-2-(1-phenylcyclopentyl)ethanoyl]-L-valyl}amino)-2-hexenoic acid,

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2R)-2-(methylamino)-2-(1-phenylcyclopentyl)ethanoyl]-L-valyl}amino)-2-hexenoic acid,

10 (2E,4R)-2,5-dimethyl-4-(methyl{3-methyl-N-[(methylamino)(1-phenylcyclohexyl)acetyl]-L-valyl}amino)-2-hexenoic acid,

(E,4S)-2,5-Dimethyl-4-[methyl((2S)-2-[[[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}-3-phenylpropanoyl]amino)-2-hexenoic acid,

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N,β,β-Trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-1-butyl-3-carboxybut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

20 N,β,β-Trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isobutyl-2-pentenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

(E,4S)-2-Butyl-4-[[[(2S)-3,3-dimethyl-2-[[[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl]amino]-5-methyl-2-hexenoic acid,

25 N,β,β-Trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-pentenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

30 Ethyl (E,4S)-2,5-dimethyl-4-{methyl[(2R)-3-methyl-2-[[[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}-3-(methylsulfanyl)butanoyl]amino]-2-hexenoate,

(E,4S)-2,5-dimethyl-4-{methyl[(2R)-3-methyl-2-[[[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}-3-(methylsulfanyl)butanoyl]amino]-2-hexenoic acid,

- N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-methyl-3-(methylsulfonyl)-L-valinamide,
- 5 N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-3-[(4-methoxybenzyl)sulfanyl]-N<sup>1</sup>-methyl-L-valinamide,
- N,O, β,β-tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-3-[(4-methoxybenzyl)sulfanyl]-N<sup>1</sup>-methyl-L-valinamide,
- 10 N,O, β,β-tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-methyl-3-(methylsulfonyl)-L-valinamide,
- N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1R,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-
- 15 butenyl]-N<sup>1</sup>-methyl-L-allothreoninamide,
- N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-methyl-L-allothreoninamide,
- 20 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N,O, β,β-tetramethyl-L-tyrosinamide,
- N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,O-dimethyl-L-allothreoninamide,
- 25 (E,4S)-2,5-Dimethyl-4-[methyl((2S)-2-[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino)-4-phenylbutanoyl]amino]-2-hexenoic acid,
- N,β,β-trimethyl-L-phenylalanyl-4-benzoyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-
- 30 2-butenyl]- N,β,β-trimethyl-L-phenylalaninamide,

- 4-benzoyl-N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,
- 5 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isobutylbut-2-enyl]-N<sup>1</sup>-methyl-L-valinamide,
- N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isobutylbut-2-enyl]-3-methyl-L-valinamide,
- 10 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>-ethyl-3-methyl-L-valinamide,
- N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>-ethyl-L-valinamide,
- 15 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>-methyl-L-leucinamide,
- N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>-methyl-L-norvalinamide,
- 20 (2E,4S)-4-[(2R)-2-cyclohexyl-2-[(N,  $\beta,\beta$ -trimethyl-L-phenylalanyl)amino]ethanoyl](methyl)amino]-2,5-dimethylhex-2-enoic acid,
- 25 (2E,4S)-2,5-dimethyl-4-(methyl[(2S)-2-[(N,  $\beta,\beta$ -trimethyl-L-phenylalanyl)amino]butanoyl]amino)hex-2-enoic acid,
- 4-[[3,3-Dimethyl-2-(2-methylamino-3-phenyl-butyrylamino)-butyryl]-methyl-amino]-2,5-dimethyl-hex-2-enoic acid,
- 30 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-methyl-L-valinamide,

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-L-valinamide,

5 2,5-dimethyl-4-{methyl-[2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-propionyl]-amino}-hex-2-enoic acid,

4-{{3,3-Dimethyl-2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-butyryl}-methyl-amino}-2,6-dimethyl-hept-2-enoic acid,

10 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-methyl-L-valinamide,

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-methyl-L-isoleucinamide,

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(E,4S)-4-[[[(2S)-3,3-dimethyl-2-[[[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino]butanoyl](methyl)amino]-2,5-dimethyl-2-hexenamide,

20 (E,4S)-4-[[[(2S)-3,3-dimethyl-2-[[[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino]butanoyl](methyl)amino]-N,2,5-trimethyl-2-hexenamide,

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-{(1S,2E)-4-[(2-cyanoethyl)amino]-1-isopropyl-3-methyl-4-oxo-2-butenyl}-N<sup>1</sup>,3-dimethyl-L-valinamide,

25 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-{(1S,2E)-4-[(carboxymethyl)amino]-1-isopropyl-3-methyl-4-oxo-2-butenyl}-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-{(1S,2E)-4-[(4-azidophenyl)amino]-1-isopropyl-3-methyl-4-oxo-2-butenyl}-N<sup>1</sup>,3-dimethyl-L-valinamide,

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N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-{(1S,2E)-1-isopropyl-3-methyl-4-oxo-4-[(2-phenylethyl)amino]but-2-enyl}-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-[[[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl](methyl)amino]-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N<sup>1</sup>-,3-dimethyl-L-valinamide,

- 5 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-[[[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl](methyl)amino]-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N<sup>1</sup>-,3-dimethyl-L-valinamide,

- 10 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-1-isopropyl-3-methyl-4-oxo-4-(thien-2-ylmethoxy)but-2-enyl]-N<sup>1</sup>-,3-dimethyl-L-valinamide,

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-1-isopropyl-3-methyl-4-(octyloxy)-4-oxobut-2-enyl]-N<sup>1</sup>-,3-dimethyl-L-valinamide,

- 15 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2Z)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-,3-dimethyl-L-valinamide,

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylprop-2-enyl]-N<sup>1</sup>-,3-dimethyl-L-valinamide,

20

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-1-allyl-3-carboxybut-2-enyl]-N<sup>1</sup>-,3-dimethyl-L-valinamide,

- 25 (2E,4S)-4-[[[(2S)-3,3-dimethyl-2-[(N, β,β-trimethyl-L-phenylalanyl)amino]-4-pentenoyl](methyl)amino]-2,5-dimethyl-2-hexenoic acid,

(2E, 4S)-4-[[[(2S)-2-[[3,3-dimethyl-2-(methylamino)-4-pentenoyl]amino]-3,3-dimethylbutanoyl](methyl)amino]-2,5-dimethyl-2-hexenoic acid,

- 30 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>-,3-dimethyl-L-isoleucinamide,

N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1R,3S)-3-carboxy-1-isopropylbutyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

5 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1R,3R)-3-carboxy-1-isopropylbutyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

$\beta,\beta$ -diethyl-N-methyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10  $\beta,\beta$ -diethyl-N-methyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

$\beta,\beta$ -dimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,  
15

O-benzyl-N-methyl-L-threonyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

20 N, $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

(2E,4S)-4-[(2S)-2-[(2S)-2-Amino-3-(1-naphthyl)propanoyl]amino]-3,3-dimethylbutanoyl(methyl)amino]-2,5-dimethyl-2-hexenoic acid,

25 N, $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>-methyl-D-valinamide,

(E,4S)-4-[(2S)-3,3-dimethyl-2-[(2S)-3-methyl-2-(methylamino)-3-(1-methyl-1H-ethyl-1H-indol-3-yl)butanoyl]amino}butanoyl)amino]-2,5-dimethyl-2-hexenoic acid,  
30

ethyl (E,4S)-4-[(2S)-3,3-dimethyl-2-[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl(methyl)amino]-2,5-dimethyl-2-hexenoate,

(E,4S)-4-(((2S)-3,3-dimethyl-2-(((2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl)amino)butanoyl)(methyl)amino]-2,5-dimethyl-2-hexenoic acid,

5 Ethyl (E,4S)-4-(((2S)-3,3-dimethyl-2-(((2R)-3-methyl-2-(methylamino)-3-phenylbutanoyl)amino)butanoyl)(methyl)amino]-2,5-dimethyl-2-hexenoate,

(E,4S)-4-(((2S)-3,3-dimethyl-2-(((2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl)amino)butanoyl)(methyl)amino]-2-methyl-5-phenyl-2-pentenoic acid,

10 (E,4S)-2,5-dimethyl-4-[methyl((2S)-2-(((2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl)amino)-3-phenylpropanoyl)amino]-2-hexenoic acid,

(4R)-4-(((2S)-2-(((2S)-2-amino-4-methylpentanoyl)amino)-3,3-dimethylbutanoyl)amino]-2,5-dimethylhexanoic acid,

15 N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-methyl-L-alpha-glutamine,

20 N,3-dimethyl-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ -trimethyl-L-tryptophyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25 3-cyclohexyl-N-methyl-L-valyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-2-(methylamino)-2-(1-phenylcyclopropyl)acetyl]-L-valyl}amino)hex-2-enoic acid,

30 (2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2R)-2-(methylamino)-2-(1-phenylcyclopropyl)acetyl]-L-valyl}amino)hex-2-enoic acid,

2-(4-[[3,3-Dimethyl-2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-butyryl]-methyl-amino]-2,5-dimethyl-hex-2-enoylamino)-4-methylsulfanyl-butyric acid methyl ester,

- 5 N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-[[[(1S)-1-carboxy-3-(methylthio)propyl]amino]-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 10 N,β,β-trimethyl-4-[(E)-2-phenylvinyl]-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,β,β-trimethyl-4-[(E)-2-phenylvinyl]-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 15 N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-fluoro-N<sup>1</sup>-methyl-D-valinamide,

N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-fluoro-N<sup>1</sup>-methyl-L-valinamide,

- 20 3-[(4-methoxybenzyl)thio]-N-methyl-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 25 N-ethyl-β,β-dimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-3-methyl-3-phenyl-2-pyrrolidin-1-ylbutanoyl]-L-valyl}amino)hex-2-enoic acid,

- 30 N-(2-hydroxyethyl)-β,β-dimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,



( $\beta$ R)-N, $\beta$ -dimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-acetyl-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-hydroxy-N<sup>1</sup>-methyl-L-valinamide, and

10 N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1R,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide  
or pharmaceutically acceptable salts thereof.

29. The method according to claim 28 wherein said compound of Formula (II) is  
15 selected from:

3-Chloro-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide ,

4-Chloro- N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

4-chloro- N, $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25 4-Chloro- N, $\beta$ , $\beta$ -triethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

4-Chloro-N,  $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide and

30 3-ethyl- N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide or pharmaceutically acceptable salts thereof.

30. The method according to Claim 28 wherein said compound of Formula (II) is selected from:

5 N,β,β,3-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,β,β,3-tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10

N,β,β,3-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,β,β,3-Tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-

15 N<sup>1</sup>,3-dimethyl-L-valinamide,

N,β,β,4-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

20 N,β,β,4-tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,β,β,4-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25

N,β,β,4-Tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,β,β,3,4-Pentamethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-

30 methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,β,β,3,4-pentamethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ ,3,4-Pentamethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 5 N, $\beta$ , $\beta$ ,3,4-Pentamethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ ,3,5-Pentamethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10

N, $\beta$ , $\beta$ ,3,5-pentamethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 15 N, $\beta$ , $\beta$ ,3,5-Pentamethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide and

N, $\beta$ , $\beta$ ,3,5-Pentamethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide  
or pharmaceutically acceptable salts thereof.

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31. The method according to claim 28 wherein said compound of Formula (II) is selected from:

- 25 N-Methyl-3-(2-thienyl)-L-valyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N-methyl-3-(2-thienyl)-D-valyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 30 N-Methyl-3-(2-thienyl)-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N-Methyl-3-(2-thienyl)-D-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

5 N-Methyl-3-thien-3-yl-L-valyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N-methyl-3-thien-3-yl-D-valyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10 N-Methyl-3-thien-3-yl-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide and

N-Methyl-3-thien-3-yl-D-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide

15 or pharmaceutically acceptable salts thereof.

32. The method according to claim 28 wherein said compound of Formula (II) is selected from:

20 3-(1-Benzothien-3-yl)-N-methylvalyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-(1-Benzothien-3-yl)-N-methylvalyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25

3-(1-Benzothien-2-yl)-N-methylvalyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide and

30 3-(1-Benzothien-2-yl)-N-methylvalyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide  
or pharmaceutically acceptable salts thereof.

33. The method according to Claim 28 wherein said compound of Formula (II) is selected from:

4-tert-Butyl-N, $\beta$ , $\beta$ -trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

4-tert-Butyl-N, $\beta$ , $\beta$ -trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10 N-Ethyl- $\beta$ , $\beta$ -dimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide and

N-Ethyl- $\beta$ , $\beta$ -dimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide

15 or pharmaceutically acceptable salts thereof.

34. The method according to claim 28 wherein said compound of Formula (II) is selected from:

20 N-(tert-Butoxycarbonyl)-N- $\beta$ , $\beta$ ,2-tetramethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,  $\beta$ , $\beta$ ,2-tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25

N,  $\beta$ , $\beta$ ,2-Tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ ,2-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-

30 N<sup>1</sup>,3-dimethyl-L-valinamide and

N, $\beta$ , $\beta$ ,2-Tetramethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide  
or pharmaceutically acceptable salts thereof.

- 5 35. The method according to claim 28 wherein said compound of Formula (II) is selected from:

3-bromo-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10

3-bromo-N, $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide and

4-bromo-N, $\beta$ , $\beta$ -trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide  
15 or pharmaceutically acceptable salts thereof.

36. The method according to claim 28 wherein said compound of Formula (II) is selected from:

20

3-phenyl-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-phenyl-N, $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide and  
25

4-phenyl-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide  
or pharmaceutically acceptable salts thereof.

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37. The method according to claim 28 wherein said compound of Formula (II) is selected from:

4-carboxy- N,β,β-trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-  
N<sup>1</sup>,3-dimethyl-L-valinamide,

- 5 3-Methoxy- N,β,β-trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-  
N<sup>1</sup>,3-dimethyl-L-valinamide and

3-Hydroxy- N,β,β-trimethylphenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-  
N<sup>1</sup>,3-dimethyl-L-valinamide

- 10 or pharmaceutically acceptable salts thereof.

38. The method according to claim 28 wherein said compound of Formula (II) is  
selected from:

- 15 N,β,β -trimethyl-3-vinyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-  
N<sup>1</sup>,3-dimethyl-L-valinamide,

N,3-Dimethyl-4-phenyl-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-  
dimethyl-L-valinamide,

20

N,3-dimethyl-4-phenyl-D-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-  
dimethyl-L-valinamide,

- 25 (2E,4S)-4-[[[(2S)-2-[[[(2S)-3,3-dimethyl-2-(methylamino)octanoyl]amino]-3,3-  
dimethylbutanoyl](methyl)amino]-2,5-dimethyl-2-hexenoic acid,

(2E,4S)-4-[[[(2S)-2-[[[(2R)-3,3-dimethyl-2-(methylamino)octanoyl]amino]-3,3-  
dimethylbutanoyl](methyl)amino]-2,5-dimethyl-2-hexenoic acid,

- 30 N,N,β,β-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-  
N<sup>1</sup>,3-dimethyl-L-valinamide and

N-(2-hydroxyethyl)-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide  
or pharmaceutically acceptable salts thereof.

- 5     39. The method according to claim 28 wherein said compound of Formula (II) is selected from:

2-Methoxy-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10

2-Methoxy-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,O, $\beta$ , $\beta$ -tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

15

N,O, $\beta$ , $\beta$ -tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 20     2-Methoxy-N,O, $\beta$ , $\beta$ -tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

2-Methoxy-N,O, $\beta$ , $\beta$ -tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25

O-isopropyl- N, $\beta$ , $\beta$ -trimethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide and

O-isopropyl- N, $\beta$ , $\beta$ -trimethyl-D-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide  
or pharmaceutically acceptable salts thereof.

30



40. The method according to claim 28 wherein said compound of Formula (II) is selected from:

3-Fluoro-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-  
5 N<sup>1</sup>,3-dimethyl-L-valinamide,

3-Fluoro- N, $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10 N, $\beta$ , $\beta$ -Trimethyl-3-(trifluoromethyl)-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ -Trimethyl-3-(trifluoromethyl)-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

15 3,5-Difluoro- N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3,5-Difluoro- N, $\beta$ , $\beta$ -trimethyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

20 N, $\beta$ , $\beta$ -trimethyl-3,5-bis(trifluoromethyl)-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide and

25 N, $\beta$ , $\beta$ -trimethyl-3,5-bis(trifluoromethyl)-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide  
or pharmaceutically acceptable salts thereof.

41. The method according to claim 28 wherein said compound of Formula (II) is  
30 selected from:

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-2-(methylanino)-2-(1-phenylcyclopentyl)ethanoyl]-L-valyl}amino)-2-hexenoic acid,

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2R)-2-(methylamino)-2-(1-phenylcyclopentyl)ethanoyl]-L-valyl}amino)-2-hexenoic acid and

- 5 (2E,4R)-2,5-dimethyl-4-(methyl{3-methyl-N-[(methylamino)(1-phenylcyclohexyl)acetyl]-L-valyl}amino)-2-hexenoic acid  
or pharmaceutically acceptable salts thereof.

42. The method according to claim 28 wherein said compound of Formula (II) is  
10 selected from:

(E,4S)-2,5-Dimethyl-4-[methyl((2S)-2-[[[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino]-3-phenylpropanoyl]amino)-2-hexenoic acid,

- 15 N, $\beta$ , $\beta$ -Trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-1-butyl-3-carboxybut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ -Trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isobutyl-2-pentenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

20

(E,4S)-2-Butyl-4-[[[(2S)-3,3-dimethyl-2-[[[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino]butanoyl]amino]-5-methyl-2-hexenoic acid,

- 25 N, $\beta$ , $\beta$ -Trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-pentenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

Ethyl (E,4S)-2,5-dimethyl-4-{methyl[(2R)-3-methyl-2-[[[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino]-3-(methylsulfanyl)butanoyl]amino]-2-hexenoate,

30

(E,4S)-2,5-dimethyl-4-{methyl[(2R)-3-methyl-2-[[[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino]-3-(methylsulfanyl)butanoyl]amino]-2-hexenoic acid,

N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-methyl-3-(methylsulfonyl)-L-valinamide,

5 N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-3-[(4-methoxybenzyl)sulfanyl]-N<sup>1</sup>-methyl-L-valinamide,

N,O, β,β-tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-3-[(4-methoxybenzyl)sulfanyl]-N<sup>1</sup>-methyl-L-valinamide and

10 N,O, β,β-tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-methyl-3-(methylsulfonyl)-L-valinamide  
or pharmaceutically acceptable salts thereof.

43. The method according to claim 28 wherein said compound of Formula (II) is  
15 selected from:

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1R,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>-methyl-L-allothreoninamide,

20 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-methyl-L-allothreoninamide,

N, β,β-trimethyl-L-phenylalanyl-N-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N,O, β,β-tetramethyl-L-tyrosinamide,

25 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,O-dimethyl-L-allothreoninamide,

(E,4S)-2,5-Dimethyl-4-[methyl((2S)-2-[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino)-4-phenylbutanoyl)amino]-2-hexenoic acid,

30 N,β,β-trimethyl-L-phenylalanyl-4-benzoyl-N-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]- N,β,β-trimethyl-L-phenylalaninamide and

4-benzoyl-N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide  
or pharmaceutically acceptable salts thereof.

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44. The method according to claim 28 wherein said compound of Formula (II) is selected from:

10 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isobutylbut-2-enyl]-N<sup>1</sup>-methyl-L-valinamide,

N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isobutylbut-2-enyl]-3-methyl-L-valinamide,

15 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>-ethyl-3-methyl-L-valinamide,

N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>-ethyl-L-valinamide,

20

N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>-methyl-L-leucinamide,

25 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>-methyl-L-norvalinamide,

(2E,4S)-4-[(2R)-2-cyclohexyl-2-[(N,  $\beta,\beta$ -trimethyl-L-phenylalanyl)amino]ethanoyl](methyl)amino]-2,5-dimethylhex-2-enoic acid,

30 (2E,4S)-2,5-dimethyl-4-(methyl{(2S)-2-[(N,  $\beta,\beta$ -trimethyl-L-phenylalanyl)amino]butanoyl}amino)hex-2-enoic acid,

4-[[3,3-Dimethyl-2-(2-methylamino-3-phenyl-butyrylamino)-butyryl]-methyl-amino]-  
2,5-dimethyl-hex-2-enoic acid,

5 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-  
enyl]-3-methyl-L-valinamide,

N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-  
enyl]-L-valinamide,

10 2,5-dimethyl-4-{methyl-[2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-  
propionyl]-amino}-hex-2-enoic acid,

4-[[3,3-Dimethyl-2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-butyryl]-methyl-  
amino]-2,6-dimethyl-hept-2-enoic acid,

15 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-  
butenyl]-N<sup>1</sup>-methyl-L-valinamide and

20 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-  
butenyl]-N<sup>1</sup>-methyl-L-isoleucinamide  
or pharmaceutically acceptable salts thereof.

45. The method according to claim 28 wherein said compound of Formula (II) is  
selected from:

25 (E,4S)-4-[[((2S)-3,3-dimethyl-2-[[((2S)-3-methyl-2-(methylamino)-3-  
phenylbutanoyl]amino)butanoyl](methyl)amino]-2,5-dimethyl-2-hexenamide,

30 (E,4S)-4-[[((2S)-3,3-dimethyl-2-[[((2S)-3-methyl-2-(methylamino)-3-  
phenylbutanoyl]amino)butanoyl](methyl)amino]-N,2,5-trimethyl-2-hexenamide,

N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-{(1S,2E)-4-[(2-cyanoethyl)amino]-1-isopropyl-3-  
methyl-4-oxo-2-butenyl}-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-[(carboxymethyl)amino]-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 5 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-[(4-azidophenyl)amino]-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-1-isopropyl-3-methyl-4-oxo-4-[(2-phenylethyl)amino]but-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-[[[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl](methyl)amino]-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 15 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-[[[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl](methyl)amino]-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 20 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-1-isopropyl-3-methyl-4-oxo-4-(thien-2-ylmethoxy)but-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-1-isopropyl-3-methyl-4-(octyloxy)-4-oxobut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

- 25 N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2Z)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide and

N, β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylprop-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide

- 30 or pharmaceutically acceptable salts thereof.

46. The method according to claim 28 wherein said compound of Formula (II) is selected from:

5 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-1-allyl-3-carboxybut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

(2E,4S)-4-[[[(2S)-3,3-dimethyl-2-[(N,  $\beta,\beta$ -trimethyl-L-phenylalanyl)amino]-4-pentenoyl](methyl)amino]-2,5-dimethyl-2-hexenoic acid,

10 N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-isoleucinamide,

N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1R,3S)-3-carboxy-1-isopropylbutyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

15

N,  $\beta,\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1R,3R)-3-carboxy-1-isopropylbutyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

20  $\beta,\beta$ -diethyl-N-methyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

$\beta,\beta$ -diethyl-N-methyl-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25 (betaS)-N,beta-dimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide and

O-benzyl-N-methyl-L-threonyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide

30 or pharmaceutically acceptable salts thereof.

47. The method according to claim 28 wherein said compound of Formula (II) is selected from:

3-Cyclohexyl-N-methyl-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-  
5 N<sup>1</sup>,3-dimethyl-L-valinamide and

3-cyclohexyl-N-methyl-L-valyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide

or pharmaceutically acceptable salts thereof.

10

48. The method according to claim 28 wherein said compound of Formula (II) is selected from:

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-2-(methylamino)-2-(1-  
15 phenylcyclopropyl)acetyl]-L-valyl}amino)hex-2-enoic acid,

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2R)-2-(methylamino)-2-(1-phenylcyclopropyl)acetyl]-L-valyl}amino)hex-2-enoic acid,

20 2-(4-{{3,3-Dimethyl-2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-butyryl]-methyl-amino}-2,5-dimethyl-hex-2-enoylamino)-4-methylsulfanyl-butyric acid methyl ester,

N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-((1S,2E)-4-{{(1S)-1-carboxy-3-(methylthio)propyl}amino}-1-isopropyl-3-methyl-4-oxobut-2-enyl)-N<sup>1</sup>,3-dimethyl-L-valinamide,  
25

N,β,β-trimethyl-4-[(E)-2-phenylvinyl]-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

30

N,β,β-trimethyl-4-[(E)-2-phenylvinyl]-D-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,



N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-fluoro-N<sup>1</sup>-methyl-D-valinamide,

5 N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-fluoro-N<sup>1</sup>-methyl-L-valinamide,

3-[(4-methoxybenzyl)thio]-N-methyl-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10 N-ethyl-β,β-dimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-3-methyl-3-phenyl-2-pyrrolidin-1-yl]butanoyl}-L-valyl)amino)hex-2-enoic acid,

15 N-(2-hydroxyethyl)-β,β-dimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

20 (βR)-N,β-dimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

3-acetyl-N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

25 N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-hydroxy-N<sup>1</sup>-methyl-L-valinamide and

N,β,β-trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1R,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide.

30 or pharmaceutically acceptable salts thereof.

49. The method according to claim 28 wherein said compound of Formula (II) is selected from:

- 5 3-Chloro-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,
- 3-bromo-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,
- 10 N, $\beta$ , $\beta$ ,3-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,
- 3-Cyclohexyl-N-methyl-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,
- 15 N,O, $\beta$ , $\beta$ -tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,
- N,O, $\beta$ , $\beta$ -tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-methyl-3-(methylsulfanyl)-L-valinamide, and
- 20 N, $\beta$ , $\beta$ ,3,4-Pentamethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide.

- 25 50. The method according to claim 28 wherein said compound of Formula (II) is N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide.

- 30 51. A method of treating, inhibiting the growth of, or eradicating a tumor in a mammal in need thereof wherein said tumor is resistant to at least one chemotherapeutic agent which method comprises providing to said mammal an effective amount of a compound selected from the group:

3-Chloro-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

5 3-bromo-N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N, $\beta$ , $\beta$ ,3-Tetramethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

10 3-Cyclohexyl-N-methyl-L-valyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

N,O,  $\beta$ , $\beta$ -tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide,

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N,O,  $\beta$ , $\beta$ -tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>-methyl-3-(methylsulfanyl)-L-valinamide, and

20 N, $\beta$ , $\beta$ ,3,4-Pentamethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide

or a pharmaceutically acceptable salt thereof.

25 52. The method according to Claim 51 wherein the chemotherapeutic agents are antimicrotubule inhibitors.

53. The method according to Claim 52 wherein the antimicrotubule inhibitors are selected from the group consisting of paclitaxel, docetaxel, vinblastine, vincristine and vinorelbine.

30

54. The method according to claim 51 wherein the tumors are selected from the group consisting of breast, colon, lung, prostate, melanoma, epidermal, leukemia,

kidney, bladder, mouth, larynx, esophagus, stomach, ovary, pancreas, liver, skin and brain.

55. The method according to Claim 51 wherein the tumors overexpress MDR-1,  
5 MXR or MRP.

56. The method according to Claim 51 wherein the resistance to chemotherapeutic agents is multiple drug resistance (MDR).

10 57. The method according to Claim 51 wherein the resistance is inherent or acquired.

58. The method according to Claim 57 wherein the resistance is acquired.

59. The method according to Claim 51 wherein a compound is administered before,  
15 concurrently, or after treatment with the chemotherapeutic agent.

60. A method of treating, inhibiting the growth of, or eradicating a tumor in a mammal in need thereof wherein said tumor is resistant to at least one chemotherapeutic agent which method comprises providing to said mammal an  
20 effective amount of the compound  
N, $\beta$ , $\beta$ -trimethyl-L-phenylalanyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N<sup>1</sup>,3-dimethyl-L-valinamide or a pharmaceutically acceptable salt thereof.

61. The method according to Claim 60 wherein the chemotherapeutic agents are  
25 antimicrotubule inhibitors.

62. The method according to Claim 61 wherein the antimicrotubule inhibitors are selected from the group consisting of paclitaxel, docetaxel, vinblastine, vincristine and vinorelbine.  
30

63. The method according to claim 60 wherein the tumors are selected from the group consisting of breast, colon, lung, prostate, melanoma, epidermal, leukemia,

kidney, bladder, mouth, larynx, esophagus, stomach, ovary, pancreas, liver, skin and brain.

64. The method according to Claim 60 wherein the tumors overexpress MDR-1,  
5 MXR or MRP.

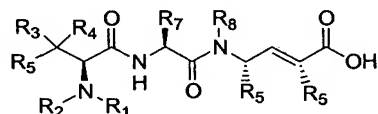
65. The method according to Claim 60 wherein the resistance to chemotherapeutic agents is multiple drug resistance (MDR).

10 66. The method according to Claim 60 wherein the resistance is inherent or acquired.

67. The method according to Claim 66 wherein the resistance is acquired.

15 68. The method according to Claim 60 wherein the compound is administered before, concurrently, or after treatment with the chemotherapeutic agent.

69. A process for the preparation of a carboxylic acid of the formula



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wherein:

25 R<sub>1</sub> is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

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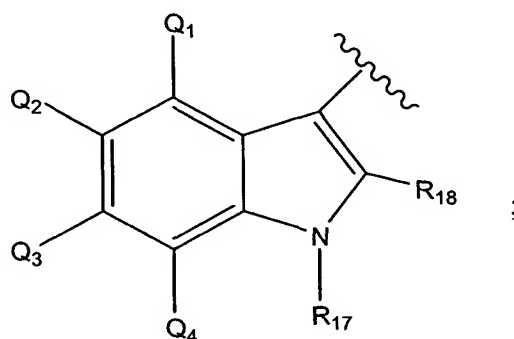
$R_2$  is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>,  
 5 -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub> or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;  
 or R<sub>1</sub> and R<sub>2</sub> taken together with the nitrogen atom to which they are attached is a  
 10 three to seven membered ring;

$R_3$  is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur  
 15 atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

$R_4$  is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur  
 20 atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and  
 25 aryl-R-;

30 or R<sub>3</sub> and R<sub>4</sub> taken together with the carbon to which they are attached form a three to seven membered ring;

$R_5$  is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R- and aryl and provided that when R<sub>5</sub> is an indolyl moiety of the formula



R<sub>17</sub> is H or an optionally substituted alkyl or acyl group; and

R<sub>18</sub> Q<sub>1</sub>, Q<sub>2</sub>, Q<sub>3</sub> and Q<sub>4</sub> are independently selected from H, halogen, alkyl, acyl, -OH, -O-alkyl, -O-acyl, -NH<sub>2</sub>, -NH-alkyl, -N(alkyl)<sub>2</sub>, -NH-acyl, -NO<sub>2</sub>, -SH, -S-alkyl and -S-acyl, wherein the alkyl and acyl groups of the substituents are optionally substituted;

R<sub>7</sub> is selected from the group consisting of a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

5  $R_8$  is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and  
 10 aryl-R-;  
 and wherein,

15 R is a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or  
 20 unsaturated alkyl group;

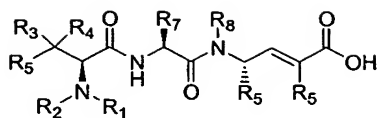
25 X is a moiety selected from the group consisting of -OH, -OR, =O, =S, -O<sub>2</sub>CR, -SH, -SR, -SOCR, -NH<sub>2</sub>, -NHR, -N(R)<sub>2</sub>, -NHCOR, NRCOR, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CO<sub>2</sub>R, -CHO, -COR, -CONH<sub>2</sub>, -CONHR, -CON(R)<sub>2</sub>, -COSH, -COSR, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR, and -SO<sub>2</sub>R;

30 Aryl is an aromatic ring selected from the group consisting of: phenyl, naphthyl, anthracyl, phenanthryl, thienyl, furyl, indolyl, pyrrolyl, thiophenyl, benzofuryl, benzothiophenyl, quinolyl, isoquinolyl, imidazolyl, thiazolyl, oxazolyl, and pyridyl, optionally substituted with R or X;

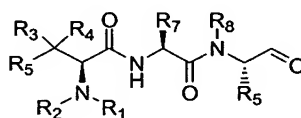
comprising the steps of:

a) treating a carboxylic acid of the formula



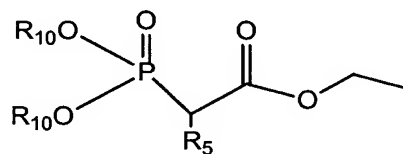


- 5 with ozone in the methanol followed by further treating with dimethylsulfide to obtain an aldehyde of the formula



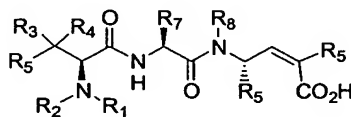
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- b) reacting said aldehyde with a phosphonate of the formula



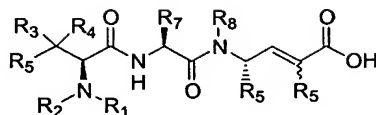
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where R<sub>10</sub> is optionally fluoro substituted alkyl of 1 to 10 carbon atoms, in the presence of potassium hexamethyldisilazide and 18-crown-6 and hydrolyzing with base to obtain a carboxylic acid of the formula



20

70. A process for the preparation of a carboxylic acid of the formula



wherein:

$R_1$  is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

$R_2$  is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, -CO<sub>2</sub>H, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub> or -SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

or  $R_1$  and  $R_2$  taken together with the nitrogen atom to which they are attached is a three to seven membered ring;

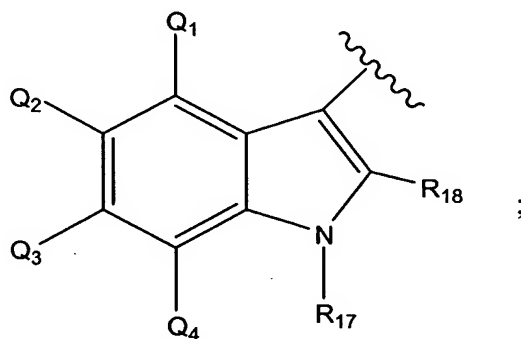
$R_3$  is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

$R_4$  is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>,  
 5 -O<sub>2</sub>CR<sub>10</sub>, -SH, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

10

or R<sub>3</sub> and R<sub>4</sub> taken together with the carbon to which they are attached form a three to seven membered ring;

$R_5$  is selected from the group consisting of H; a saturated or unsaturated  
 15 moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH,  
 20 -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R- and aryl and provided that when R<sub>5</sub> is an indolyl moiety of the formula



25

R<sub>17</sub> is H or an optionally substituted alkyl or acyl group; and

R<sub>18</sub> Q<sub>1</sub>, Q<sub>2</sub>, Q<sub>3</sub> and Q<sub>4</sub> are independently selected from H, halogen, alkyl, acyl, -OH, -O-alkyl, -O-acyl, -NH<sub>2</sub>, -NH-alkyl, -N(alkyl)<sub>2</sub>, -NH-acyl, -NO<sub>2</sub>, -SH, -S-alkyl and -S-acyl, wherein the alkyl and acyl groups of the substituents are optionally substituted;

5

R<sub>7</sub> is selected from the group consisting of a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>,  
 10 -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

15

R<sub>8</sub> is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR<sub>10</sub>,  
 20 -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or -SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

25 and wherein,

R is a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally  
 30 substituted with: =O, =S, OH, -OR<sub>10</sub>, -O<sub>2</sub>CR<sub>10</sub>, -SH, -SR<sub>10</sub>, -SOCR<sub>10</sub>, -NH<sub>2</sub>, -NR<sub>10</sub>H, -N(R<sub>10</sub>)<sub>2</sub>, -NHCOR<sub>10</sub>, -NR<sub>10</sub>COR<sub>10</sub>, -I, Br, -Cl, -F, -CN, CO<sub>2</sub>H, -CO<sub>2</sub>R<sub>10</sub>, -CHO, -COR<sub>10</sub>, -CONH<sub>2</sub>, -CONHR<sub>10</sub>, -CON(R<sub>10</sub>)<sub>2</sub>, -COSH, -COSR<sub>10</sub>, -NO<sub>2</sub>, -SO<sub>3</sub>H, -SOR<sub>10</sub>, or

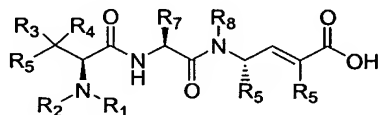
$-\text{SO}_2\text{R}_{10}$  wherein  $\text{R}_{10}$  is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group;

X is a moiety selected from the group consisting of  $-\text{OH}$ ,  $-\text{OR}$ ,  $=\text{O}$ ,  $=\text{S}$ ,  
 5  $-\text{O}_2\text{CR}$ ,  $-\text{SH}$ ,  $-\text{SR}$ ,  $-\text{SOCR}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}$ ,  $-\text{N}(\text{R})_2$ ,  $-\text{NHCOR}$ ,  $\text{NRCOR}$ ,  $-\text{I}$ ,  $\text{Br}$ ,  $-\text{Cl}$ ,  $-\text{F}$ ,  
 $-\text{CN}$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{CO}_2\text{R}$ ,  $-\text{CHO}$ ,  $-\text{COR}$ ,  $-\text{CONH}_2$ ,  $-\text{CONHR}$ ,  $-\text{CON}(\text{R})_2$ ,  $-\text{COSH}$ ,  $-\text{COSR}$ ,  
 $-\text{NO}_2$ ,  $-\text{SO}_3\text{H}$ ,  $-\text{SOR}$ , and  $-\text{SO}_2\text{R}$ ;

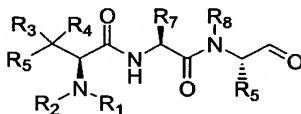
Aryl is an aromatic ring selected from the group consisting of: phenyl,  
 10 naphthyl, anthracyl, phenanthryl, thienyl, furyl, indolyl, pyrrolyl, thiophenyl,  
 benzofuryl, benzothiophenyl, quinolyl, isoquinolyl, imidazolyl, thiazolyl, oxazolyl, and  
 pyridyl, optionally substituted with R or X;

comprising the steps of:

15 b) treating a carboxylic acid of the formula

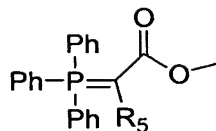


with ozone in methanol followed by further treating with dimethylsulfide to obtain an  
 20 aldehyde of the formula

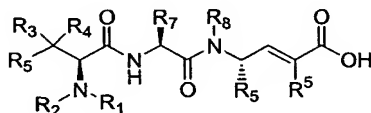


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c) reacting said aldehyde of step a) with triphenylphosphorane of the formula



and hydrolyzing with base to obtain said carboxylic acid having the formula



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71. The process according to Claim 69 wherein the base in step b) is aqueous lithium hydroxide.

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72. The process according to Claim 70 wherein the base in step b) is aqueous lithium hydroxide.

73. A method of treating, inhibiting the growth of, or eradicating a tumor in a mammal in need thereof wherein said tumor is resistant to at least one chemotherapeutic agent which method comprises providing to said mammal an effective amount of the compound

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N,O, $\beta$ , $\beta$ -tetramethyl-L-tyrosyl-N<sup>1</sup>-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N<sup>1</sup>,3-dimethyl-L-valinamide.

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74. The method according to Claim 73 wherein the chemotherapeutic agents are antimicrotubule inhibitors.

75. The method according to Claim 74 wherein the antimicrotubule inhibitors are selected from the group consisting of paclitaxel, docetaxel, vinblastine, vincristine and vinorelbine.

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76. The method according to Claim 73 wherein the tumors are selected from the group consisting of breast, colon, lung, prostate, melanoma, epidermal, leukemia,

kidney, bladder, mouth, larynx, esophagus, stomach, ovary, pancreas, liver, skin and brain.

5 77. The method according to Claim 73 wherein the tumors overexpress MDR-1, MXR or MRP.

78. The method according to Claim 73 wherein the resistance to chemotherapeutic agents is multiple drug resistance (MDR).

10 79. The method according to Claim 73 wherein the resistance is inherent or acquired.

80. The method according to Claim 79 wherein the resistance is acquired.

15 81. The method according to Claim 73 wherein the compound is administered before, concurrently, or after treatment with the chemotherapeutic agent.

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